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European Patent

EP 0,780,114 A1

Siliconized Surfactant-based Transparent Nanoemulsion and Its Use in Cosmetics or Dermopharmacy

[Nanoémulsion transparente à base de tensioactifs siliconés et utilisation en cosmétique ou en dermopharmacie]

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Description

The present invention relates to a transparent oil-in-water emulsion whose oil globules have an average size that is smaller than 100 nm and that includes at least one siliconized surfactant, and to its use in topical applications, specifically in the cosmetic and dermatological fields.

Oil-in-water emulsions, wherein an oily phase is dispersed in an aqueous phase, are well known in the cosmetic field and in dermopharmacy, especially in the preparation of products such as lotions, tonics, serums, creams, and eau de toilette.

In order to obtain transparent compositions whose appearance is close to that of water and that produce, after they are applied to the skin, a feel analogous to a cream or to a lotion, we have implemented emulsions that include oil globules whose average size is smaller than 100 nm, referred to as nanoemulsions.

Hence, the document EP-A-406162 describes nanoemulsions including an amphiphilic phase composed of phosphoglycerides. These nanoemulsions are obtained via a high-pressure homogenization method. They have the disadvantage of being

[1] Numbers in the margin indicate pagination in the foreign text.

unstable for storage at conventional storage temperatures, namely between 0 and 45°C and therefore lead to yellow compositions that give off rancid odors developing after a few days of storage.

Additionally, the document EP-A-615741 describes nanoemulsions including the association of a fatty alcohol and/or a long-chain fatty acid with a surfactant of the long-chain fatty-acid soap type, forming a phase transition temperature gel that is higher than 60°C. These nanoemulsions are prepared at temperatures above 70°C, which makes it impossible to use heat-sensitive active ingredients (vitamins, for example) in such compositions.

The need remains, therefore, for a nanoemulsion that does not involve the disadvantages encountered with those known to date.

The nanoemulsion of the invention eliminates the problems mentioned above. Indeed, the applicant has discovered - to his surprise - that it is possible to obtain a stable nanoemulsion that can be prepared at temperatures between 20 and 45°C by using a specific surfactant.

The object of the present invention is therefore an oil-in-water nanoemulsion including an oily phase dispersed in an aqueous phase, whose oil globules have an average size that is

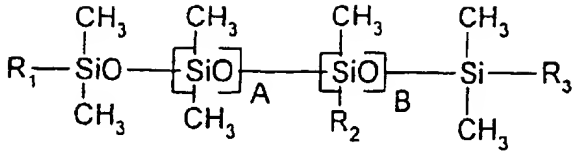
smaller than 100 nm, wherein it includes at least one siliconized surfactant.

The emulsions in accordance with the invention, whose oil globules have an average size that is smaller than 100 nm are stable during storage between 0 and 45°C after at least two months have elapsed. They are prepared at temperatures ranging from 20 to 45°C; therefore, it is possible to add heat-sensitive active ingredients to them without harming the nanoemulsions; such ingredients include, for example, vitamins and vegetable oils containing unsaturated fatty acids.

Additionally, the emulsions of the invention can contain considerable quantities of oil while retaining good transparency properties. Moreover, they encourage the penetration of active ingredients into the superficial layers of the skin.

A siliconized surfactant is a siliconized compound that includes at least one oxyethylenated $-OCH_2CH_2-$ chain and/or one oxypropylenated $-OCH_2CH_2CH_2-$ chain. As siliconized surfactants that can be used according to the present invention, we may cite those described in the documents US-A-5364633 and US-A-5411744.

Preferably, the siliconized surfactant used according to the present invention is a formula (I) compound:



(I)

wherein:

R_1, R_2, R_3, each independent of the others, represent a C_1-C_6 alkyl radical or a $-(CH_2)_x - (OCH_2CH_2)_y - (OCH_2CH_2CH_2)_z - OR_4$ radical, with at least one R_1, R_2, or R_3 radical not being an alkyl radical; R_4 being a hydrogen, an alkyl radical, or an acyl radical;

A is a whole number ranging from 0 to 200;

B is a whole number ranging from 0 to 50; provided that A and B are not equal to zero at the same time;

x is a whole number ranging from 1 to 6;

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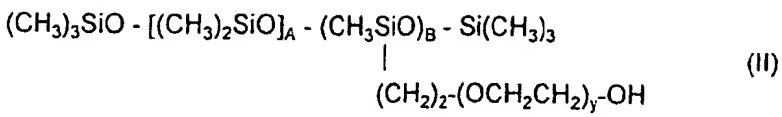
y is a whole number ranging from 1 to 30;

z is a whole number ranging from 0 to 5.

According to a preferred embodiment of the invention, in the compound of Formula (I), the alkyl radical is a methyl radical, x is a whole number ranging from 2 to 6, and y is a whole number ranging from 4 to 30.

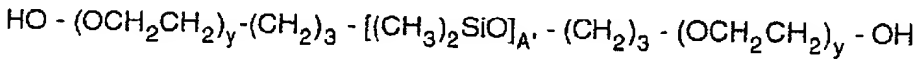
As examples of Formula (I) siliconized surfactants, we may cite the compounds of Formula (II):



(II)

wherein A is a whole number ranging from 20 to 105, B is a whole number ranging from 2 to 10, and y is a whole number ranging from 10 to 20.

As examples of Formula (I) siliconized surfactants, we may also cite the compounds of Formula (III):



(III)

wherein A' and y are whole numbers ranging from 10 to 20.

As compounds of the invention, those sold by the Dow Corning Corporation under the denominations DC 5329, DC 7439-146, DC 2-5695, and Q4-3667 may be used. The compounds DC 5329, DC 7439-146, and DC 2-5695 are Formula (II) compounds wherein, respectively, A is 22, B is 2, and y is 12; A is 103, B is 10, and y is 12; A is 27, B is 3, and y is 12.

The compound Q4-3667 is a Formula (III) compound wherein A is 15 and y is 13.

The weight ratio of the oily phase quantity contained in the emulsion of the invention to the siliconized surfactant quantity varies, preferably from 2 to 10, and even more preferably from 3 to 6.

The quantity of siliconized surfactant in the emulsion of the invention ranges, preferably, from 1 to 15% by weight, and better still from 3 to 6% by weight in relation to the emulsion's total weight.

The emulsion in accordance with the invention includes a quantity of oily phase that ranges, preferably, from 5 to 40% by weight, and even more preferably from 10 to 30% by weight in relation to the emulsion's total weight.

As oils that can be used in the invention, we may cite mineral oils (vaseline oil), vegetable oils (liquid fraction of shea butter, sunflower oil), animal oils (perhydrosqualene), synthetic oils (PurCellin oil), natural or synthetic essential oils (oils of eucalyptus, lavandin, lavender, vetiver, litsea cubeba, lemon, sandalwood, rosemary, chamomile, savory, nutmeg, cinnamon, hyssop, caraway, orange, geraniol, Spanish juniper, and bergamot), volatile siliconized oils (decamethylcyclopentasiloxane) or non-volatile siliconized oils (dodecamethylcyclohexasiloxane), fluorinated oils (perfluoropolyethers), halogenated carbides (fluorocarbides such as fluoramines; for example, perfluorotributylamine; fluorinated hydrocarbides, for example, perfluorodecahydronaphthalene). One may also use fatty alcohols, fatty acids, waxes, and gums (silicone gum) as fats.

According to a specific embodiment of the invention, the emulsion of the invention also contains one or several ionic amphiphilic lipids.

The ionic amphiphilic lipids used in the nanoemulsions of the invention are preferably selected from among the group formed by neutralized anionic lipids, amphoteric ionic lipids, and alkylsulfonic derivatives.

More specifically, they are selected from the group formed by:

- the alkaline salts of dicetyl- and dimyristylphosphate;
- the alkaline salts of cholesterol sulfate;
- the alkaline salts of cholesterol phosphate;
- lipoaminoacids such as mono- and disodium acylglutamates;
- the sodium salts of phosphatidic acid;
- phospholipids;
- alkylsulfonic derivatives of the formula:

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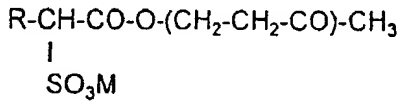

wherein R represents C_{16}-C_{22} alkyl radicals, specifically the $C_{16}H_{33}$ and $C_{18}H_{37}$ radicals, whether as a mixture or separately, and M is an alkaline metal such as sodium and potassium;

- and their mixtures.

As ionic amphiphilic lipids, we may cite in particular the monosodium salt of N-stearoylglutamic acid sold as "acylglutamate HS 21" by the Ajinomoto Company, sodium dicetylphosphate, and sodium dimyristylphosphate.

More specifically, the amphiphilic ionic lipids are present in concentrations ranging from 0 to 20% by weight, even more specifically from 5 to 15% by weight in relation to the weight of the siliconized surfactant.

The emulsion according to the present invention may contain additives in order to improve the formulation's transparency.

These additives may be selected, for example, from the group formed by:

- C_1-C_8 lower alcohols, such as ethanol;
- glycols, such as glycerin, propylene glycol, 1,3-butylene glycol, dipropylene glycol, polyethylene glycols including 4 to 16 units of ethylene oxide, preferably 8 to 12;
- and their mixtures.

The additives such as those cited above are preferably used in the emulsion of the invention in concentrations ranging from 0 to 30% by weight, preferably in a concentration greater than 5% by weight in relation to the emulsion's total weight. The alcohols are preferably used in concentrations ranging from 5 to

20% by weight in relation to the emulsion's total weight, whereas the glycols are preferably used in concentration ranging from 5 to 15% by weight.

Moreover, the use of alcohols as defined above in concentrations greater than or equal to 15% by weight makes it possible to obtain preservative-free emulsions.

The oil globules of the emulsions of the invention preferably have an average size ranging from 15 to 100 nm, more preferably from 15 to 90 nm. The decreased size of the globules encourages penetration of active ingredients into the superficial layers of the skin (vehicle effect) and improves the emulsion's transparency.

The emulsions of the invention are colorless, with possibly a slight bluish tinge, and have a transparency level determined by the U-value measured at a 600-nm wavelength, preferably ranging from 30 to 90%, more specifically from 50 to 80%.

The method for obtaining the emulsions of the invention includes the following steps:

- the aqueous phase and the oily phase are mixed while stirring briskly at an ambient temperature below 45°C;
- high-pressure homogenization is performed at a pressure above 10^8 Pa, preferably between 12.10^7 and 18.10^7 Pa.

This type of method makes it possible to make, at ambient temperature, nanoemulsions that are compatible with heat-sensitive active ingredient compounds. Additionally, these nanoemulsions may contain considerable quantities of oils, specifically perfumes including fatty bodies, without denaturing them.

For a topical application, the emulsion of the invention additionally contains, advantageously, a cosmetically- and/or dermatologically- and/or pharmaceutically-acceptable medium.

Another object of the invention is the use of the emulsion defined above for cosmetic treatment of the skin and/or of the mucous membranes and/or of the nails and/or of the scalp and/or of the hair, as well as for the preparation of a composition to be used in dermatological treatment of disorders of the skin and/or of the mucous membranes and/or of the nails and/or of the scalp and/or of the hair.

Yet another object of the invention is a method for therapeutic and/or nontherapeutic treatment of the skin and/or of the mucous membranes and/or of the nails and/or of the scalp and/or of the hair that consists of applying the emulsion defined above onto the skin and/or the mucous membranes and/or the nails and/or the scalp and/or the hair.

In particular, the emulsion provides good skin moisturizing and enables treatment of oily skin and sensitive skin. Thus, the present invention also relates to the use of the emulsion defined above in order to moisturize the skin and/or to treat oily skin and/or to treat sensitive skin. For the definition of "sensitive skin," refer to the document EP-A-680749.

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The emulsion of the invention may take the form of a lotion, serum, or gel, and may contain adjuvants normally used in the relevant fields, such as gelling agents, preservatives, antioxidants, fragrances, fillers, coloring agents, and lipid vesicles.

The emulsion of the invention may constitute compositions for cleaning, protecting, treating, or caring for the face, neck, hands, nails, or body (for example, cleaning lotion, makeup removing lotion, body lotion), artificial tanning compositions, or bath or shower compositions. The emulsion of the invention may also constitute shampoos, hairstyling lotions, conditioning lotions, hairstyling creams or gels, hair coloring compositions, and hairspray lotions or gels.

The emulsion of the invention may contain hydrosoluble or liposoluble active ingredients that have cosmetic or dermatological activity. The liposoluble active ingredients are

in the oil globules of the emulsion, while the hydrosoluble active ingredients are in the aqueous phase of the emulsion. As a liposoluble active ingredient, we may cite, for example, retinol (vitamin A) and its derivatives such as retinol palmitate.

The following examples will, in non-limiting fashion, allow the invention to be more fully understood.

For these examples, the following method of operation is used:

- in an initial phase A, the mixture of constituents is homogenized at a temperature of 45°C;
- in a second phase B, the active ingredients and hydrophilic adjuvants are dissolved at a temperature of 20 to 30°C;
- then phases A and B are mixed using a turbine homogenizer, and next they are homogenized using a high-pressure homogenizer of the Soavi-Niro type at a pressure of 1500 bars, in 7 passes, while keeping the temperature of the product below 30°C.

If ethanol is present in the composition, it is added during phase A immediately before the latter is added to phase B.

Example 1: Fluid for Care of Oily Skin

Initial Phase:

- Siliconized surfactant (DC 2-5695) 5%

- Dodecamethylcyclohexasiloxane 6%
- Decamethylcyclopentasiloxane 6%
- Silicone gum (Q2-1403 sold by Dow Corning) 3%
- Non-denatured absolute ethanol 15%

Second Phase:

- Glycerin 5%
- Demineralized water qsp. 100%

A transparent emulsion is obtained; the size of its oil globules is 52 nm, with a transparency level determined by the U-value at 600 nm, equal to 80%.

This fluid emulsion is cool to the skin upon application.

Example 2: Fluid for Care of Sensitive Skin

Initial Phase:

- Siliconized surfactant (DC 2-5695) 5%
- Decamethylcyclopentasiloxane 6%
- Perhydrosqualene 6%
- Silicone gum (Q2-1403 sold by Dow Corning) 3%

Second Phase:

- Glycerin 5%

- Dipropylene glycol 10%
- Demineralized water qsp. 100%

A pearly emulsion is obtained; the globule size is 70 nm and the transparency is 40%. This fluid emulsion has a mild feel upon application and is appropriate for treating sensitive skin.

Example 3: Fluid for Daytime Skin Care

Initial Phase:

- Siliconized surfactant (DC 2-5695) 4.5%
- Disodium salt of N-stearoyl L-glutamic acid, sold as Acylglutamate HS21 by the Ajinomoto Company (ionic amphiphilic lipid) 0.5%
- Cyclomethicone 6%
- Jojoba oil 6%
- Avocado oil 3%
- Retinol palmitate 0.3%
- Nondenatured absolute ethanol 15%

Second Phase:

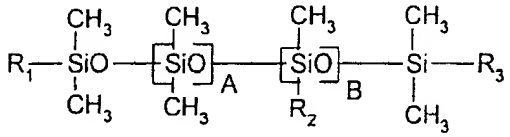
- Glycerin 5%
- Demineralized water qsp. 100%

A transparent emulsion is obtained whose globule size is 57 nm and whose transparency is 67%. This fluid emulsion is appropriate for treating the skin.

Claims

1. Oil-in-water emulsion including an oily phase dispersed in an aqueous phase, whose oil globules have an average size that is smaller than 100 nm, wherein it includes at least one siliconized surfactant.

2. Emulsion according to Claim 1, wherein the siliconized surfactant is a compound of Formula (I):



(I)

wherein

R_1, R_2, R_3, each independent of the others, represent a C_1-C_6 alkyl radical or a $-(CH_2)_x - (OCH_2CH_2)_y - (OCH_2CH_2CH_2)_z - OR_4$ radical, with at least one R_1, R_2, or R_3 radical not being an alkyl radical; R_4 being a hydrogen, an alkyl radical, or an acyl radical;

A is a whole number ranging from 0 to 200;

B is a whole number ranging from 0 to 50; provided that A and B are not equal to zero at the same time;

x is a whole number ranging from 1 to 6;

y is a whole number ranging from 1 to 30;

z is a whole number ranging from 0 to 5.

3. Emulsion according to Claim 2, wherein the siliconized surfactant is a Formula (I) compound where the alkyl radical is a methyl radical, x is a whole number ranging from 2 to 6, and y is a whole number ranging from 4 to 30.

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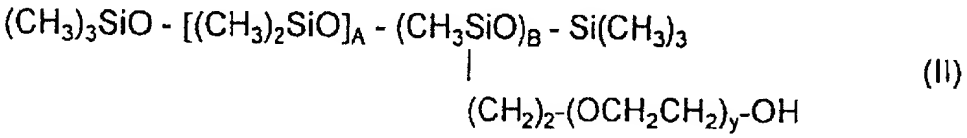
4. Emulsion according to any of the preceding claims, wherein the siliconized surfactant is a compound of Formula (II):

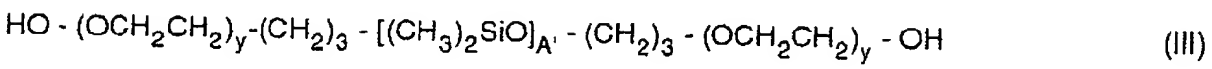


(II)

wherein A is a whole number ranging from 20 to 105, B is a whole number ranging from 2 to 10, and y is a whole number ranging from 10 to 20.

5. Emulsion according to the preceding claim, wherein the siliconized surfactant is selected from among the Formula (II) compounds wherein A is 22, B is 2, and y is 12; A is 103, B is 10, and y is 12; A is 27, B is 3, and y is 12.

6. Emulsion according to any of claims 1 through 3, wherein the siliconized surfactant is a compound of Formula (III):



$$HO-(OCH_2CH_2)_y-(CH_2)_3-[(CH_3)_2SiO]_{A'}-(CH_2)_3-(OCH_2CH_2)_y-OH \qquad (III)$$

wherein A' and y are whole numbers ranging from 10 to 20.

7. Emulsion according to the preceding claim, wherein the siliconized surfactant is a compound of Formula (III) wherein A is 15 and y is 13.

8. Emulsion according to any of the preceding claims, wherein the weight ratio of the quantity of oily phase to the quantity of siliconized surfactant ranges from 2 to 10.

9. Emulsion according to any of the preceding claims, wherein the quantity of siliconized surfactant ranges from 1 to 15% by weight in relation to the emulsion's total weight.

10. Emulsion according to any of the preceding claims, wherein the quantity of siliconized surfactant ranges from 3 to 6% by weight in relation to the emulsion's total weight.

11. Emulsion according to any of the preceding claims, wherein the oily phase is present in a quantity ranging from 5 to 40% by weight in relation to the emulsion's total weight.

12. Emulsion according to any of the preceding claims, wherein the oily phase is present in a quantity ranging from 10 to 30% by weight in relation to the emulsion's total weight.

13. Emulsion according to any of the preceding claims, wherein it additionally contains at least one ionic amphiphilic lipid.

14. Emulsion according to the preceding claim, wherein the ionic amphiphilic lipid is selected from among the group formed by neutralized anionic lipids, amphoteric ionic lipids, alkylsulfonic derivatives, and their mixtures.

15. Emulsion according to Claim 13 or 14, wherein the ionic amphiphilic lipid is selected from the group formed by:

- the alkaline salts of dicetyl- and dimyristylphosphate;
- the alkaline salts of cholesterol sulfate;
- the alkaline salts of cholesterol phosphate;
- lipoaminoacid salts;
- the sodium salts of phosphatidic acid;
- phospholipids;

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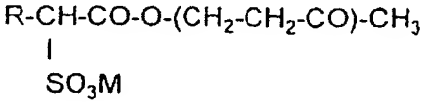
- alkylsulfonic derivatives of the formula:



wherein R represents C_{16}-C_{22} alkyl radicals, whether as a mixture or separately, and M is an alkaline metal,

- and their mixtures.

16. Emulsion according to any of claims 13 through 15, wherein the ionic amphiphilic lipid is present in concentrations ranging from 5 to 15% by weight in relation to the weight of siliconized surfactant.

17. Emulsion according to any of the preceding claims, wherein the oily phase includes at least one siliconized oil and/or one siliconized gum.

18. Emulsion according to any of the preceding claims, wherein the size of the particles is such that the emulsion is transparent.

19. Emulsion according to any of the preceding claims, wherein it contains an additive that improves transparency.

20. Emulsion according to the preceding claim, wherein the additive is selected from among lower alcohols, glycols, and their mixtures.

21. Emulsion according to Claim 19 or 20, wherein the additive is present in concentration ranging from 5 to 30% by weight in relation to the emulsion's total weight.

22. Emulsion according to any of the preceding claims, wherein the oil globules have an average size ranging from 15 to 90 nm.

23. Emulsion according to any of the preceding claims, wherein it consists of a cosmetic and/or dermatological composition.

24. Emulsion according to any of the preceding claims, wherein it contains a hydrosoluble or liposoluble cosmetic or dermatological active ingredient.

25. Use of the emulsion according to any of the preceding claims for cosmetic treatment of the skin and/or mucous membranes and/or nails and/or scalp and/or hair.

26. Use of the emulsion according to any of claims 1 through 24 for the preparation of a composition to be used in dermatological treatment of disorders of the skin and/or mucous membranes and/or nails and/or scalp and/or hair.

27. Use of the emulsion according to any of claims 1 through 24 in order to moisturize the skin and/or to treat oily skin and/or to treat sensitive skin.

28. Method for nontherapeutic treatment of the skin and/or mucous membranes and/or nails and/or scalp and/or hair, wherein it consists of applying the emulsion according to any of claims

1 through 24 onto the skin and/or mucous membranes and/or nails and/or scalp and/or hair.

European Patent Office

EUROPEAN SEARCH REPORT

Application No.: EP 96,40,2548

PERTINENT DOCUMENTS			
Category	Document citation with indication, if necessary, of pertinent sections	Claim involved	Grading of the request (Int.Cl.5)
A	EP 0,638,308 A (DOW CORNING CORPORATION) * page 6 - page 7; claims *	1-28	A61K7/00 A61K7/48
A	EP 0,529,847 A (DOW CORNING CORPORATION) * page 12 - page 13; claims *	1-28	
A	EP 0,407,089 A (UNILEVER N.V.) * page 9 - page 10; claims *	1-28	
A	EP 0,514,934 A (DOW CORNING CORPORATION) * page 22 - page 23; claims *	1-28	
A	EP 0,226,337 A (ELI LILLY AND COMPANY) * page 37 - page 46; claims *	1-28	
A	TENSIDE, SURFACTANT, DETERGENTS, Vol. 29, No. 2, March 1992, MUNICH, Pages 78-83, XP000262468 B. GRÜNING ET AL:	1-28	
A	EP 0,631,774 A (TH. GOLDSCHMIDT AG) * page 9 - page 10; claims *	1-28	Technical fields searched (Int.Cl.6)
A	EP 0,559,013 A (TH. GOLDSCHMIDT AG) * page 11; claims *	1-28	A61K
A	EP 0,330,369 a (RICHARDSON-VICKS, INC.) * page 8; claims *	1-28	
A	FR 2,693,466 A (L'ORÉAL) * page 26 - page 29; claims *	1-28	
A	EP 0,579,455 A (DOW CORNING CORPORATION) * page 13; claims *	1-28	

A	FR 2,683,453 A (YVES SAINT LAURENT PARFUMS) * page 6 - page 7; claims *	1-28	
The present report has been established for all claims			
Place of search: The Hague	Date search completed: March 6th 1997	Examiner: Luyten, H.	

CATEGORY OF THE CITED DOCUMENTS X: Especially pertinent on its own Y: Especially pertinent in combination with another document in the same category A: Technological background O: Unwritten disclosure P: Intermediate document	T: Theory or principle on which the invention is based E: Prior patent document, but published on the filing date or after this date D: Cited in the application L: Cited for other reasons A: Member of the same family, corresponding document

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EUROPEAN SEARCH REPORT

Application No.: EP 96,40,2548

PERTINENT DOCUMENTS			
Category	Document citation with indication, if necessary, of pertinent sections	Claim involved	Grading of the request (Int.Cl.6)
A	FR 2,315,991 A (L'ORÉAL) * page 16 - page 20; claims *	1-28	
A	FR 2,597,367 A (L'ORÉAL) * page 21 - page 25; claims *	1-28	
A	FR 2,597,345 A (L'ORÉAL) * page 24 - page 28; claims *	1-28	
D,A	US 5,364,633 A (RANDAL M. HILL ET AL) * entire document *	1-28	
D,A	EP 0,406,162 A (WEDER, HANS GEORG PROF. DR.) * entire document *	1-28	
D,A	EP 0,615,714 A (SHISEIDO COMPANY LIMITED) * entire document *	1-28	

			Technical fields searched (Int.Cl.6)
The present report has been established for all claims			
Place of search: The Hague	Date search completed: March 6th, 1997	Examiner: Luyten, H.	

CATEGORY OF THE CITED DOCUMENTS	
X: Especially pertinent on its own	T: Theory or principle on which the invention is based
Y: Especially pertinent in combination with another document in the same category	E: Prior patent document, but published on the filing date or after this date
A: Technological background	D: Cited in the application
O: Unwritten disclosure	L: Cited for other reasons
P: Intermediate document	A: Member of the same family, corresponding document